BIOTRONIK - Safety and Clinical Performance of the Drug Eluting Absorbable Metal Scaffold (DREAMS 2nd Generation) in the Treatment of Subjects with de Novo Lesions in Native Coronary Arteries: BIOSOLVE-II

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Assessment of safety and clinical performance of the DREAMS 2nd Generation in de novo coronary artery lesions.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON46947

Source
ToetsingOnline

Brief title
BIOSOLVE-II

Condition

- Coronary artery disorders

Synonym
coronary stenosis, narrowing of the vessels (arteries) which supply the heart with blood

Research involving
Human

Sponsors and support

Primary sponsor: Biotronik
Source(s) of monetary or material Support: BIOTRONIK AG

Intervention

Keyword: coronary artery disease, DREAMS, drug-eluting absorbable metal scaffold

Outcome measures

Primary outcome

Primary endpoint will be in-segment late lumen loss (LLL) at 6-month

post-procedure.

Secondary outcome

Clinical

• Target Lesion Failure (TLF; composite of Cardiac Death, Target Vessel Q-wave

or non-Q wave Myocardial Infarction (MI), Coronary Artery Bypass Grafting

(CABG), clinically driven Target Lesion Revascularization (TLR)) at 1, 6, 12,

24, 36 and 60-month

• Scaffold thrombosis rate at 1, 6, 12, 24, 36 and 60-month (according to ARC

definition)

• Procedure success and device Success

Angiographic

• Binary in-scaffold and in-segment restenosis rate at 6, 12 and 36-month

• % in-scaffold and in-segment diameter stenosis at 6, 12 and 36-month

• Late lumen loss in-scaffold at 6, 12 and 36-month and in-segment at 12 and

36-month

OCT and IVUS

• Descriptive analysis of vessel morphology, lesion composition and scaffold

strut data

Vasomotion

• Descriptive analysis of vessel movement

Study description

Background summary

Drug-eluting stents (DES) have reduced restenosis rates compared to bare metal stents (BMS) for the treatement of atheriosclerosis but have been associated with a risk of late thrombotic events. These complications could be limited by prolonged dual antiplatelet therapy (DAPT), but are still an issue with an annual rate of 0.5-0.8%
Bioabsorbable vascular scaffolds (BVS) have been developed to overcome the limitations of permanent bare metal or drug eluting stents, to reduce the rate of stent thrombosis, aiming for a reduced duration of DAPT, to avoid creation of a permanently caged vessel and improved vasomotion and vessel remodeling, and to avoid chronic vessel wall inflammation. Furthermore a scaffold provide improved non-invasive vessel lumen imaging by computer tomography or magnetic resonance technology and facilitate surgical or interventional target vessel and lesion reintervention.
Currently two different scaffolds technologies are under development, on one hand scaffolds consisting of absorbable metal like for instance our device DREAMS consisting of Magensium with the advantage of mechanical performance comparable to a permanent stent and on the other hand polymeric scaffolds. Up to now two different polymeric scaffolds are available on the market with comparable performace to a permanent stent as was seen in clinical studies.
Within the scope of the development of the DREAMS scaffold, earlier versions have been implanted in about 120 patients to date and its safety was evaluated in several animal trials. Clinical trials with two earlier versions demonstrated a good safety profile but the late lumen loss and revascularization rates were relatively high.
To achieve a comparable performace like a contemporary DES the DREAMS scaffold was refined incorporating a more flexible, stronger scaffold backbone design with higher radial force and the exchange of the drug to a more potent inhibitor of neointima growth. This new version will be evaluated for the first

time in humans within this clinical study.

Study objective

Assessment of safety and clinical performance of the DREAMS 2nd Generation in de novo coronary artery lesions.

Study design

Up to 121 subjects will be enrolled in this prospective, multi-centre, first in man trial. Clinical follow-up visits will take place at 1, 6, and 12 months and annually thereafter until 3 years post procedure and at 5 years post procedure if subjects consent for the prolongation of follow-up time up to 5 years If a patient passed away between the 3 year and 5 year follow-up and could not give the additional informed consent, the date and cause of death should be captured. These data will not be used in the final analysis, but an overview should be presented indicating the reason for which patients did not take part in the prolongation of the study.
All subjects will undergo an angiographic follow-up at 6-month. Additional imaging methods will be performed IVUS (including additional IVUS-VH analysis) and OCT for a subset of up to 30 evaluable patients. An additional voluntary imaging follow-up will be performed at 12-month follow-up and 3 years. Vasomotion will be assessed angiographically with Acetylcholine followed by Nitroglycerine, if subject consents.

Intervention

Percutaneous transluminal coronary angioplasty (PTCA) including concomitant anticoagulation medication according to protocol and implantation of the DREAMS scaffold. For a subgroup of patients IVUS and OCT for additional imaging after scaffold implantation will be performed.

Study burden and risks

As with any subject undergoing percutaneous coronary intervention, subjects may experience adverse events and/or outcomes that may include, but are not necessarily limited to the following:

Cardiac events:
Myocardial infarction or ischemia, abrupt closure of coronary artery, restenosis of treated artery (greater than 50% obstruction), cardiogenic shock, angina, tamponade, perforation or dissection of coronary artery or aorta, cardiac perforation, emergency cardiac surgery, pericardial effusion, aneurysm formation, death.

Arrhythmic events:

Ventricular tachycardia, ventricular fibrillation, atrial fibrillation, bradycardia.

Scaffold system events:
Failure to deliver scaffold to intended site, scaffold dislodgement from the delivery system, scaffold misplacement, scaffold deformation, scaffold embolization, scaffold thrombosis or occlusion, scaffold fracture, scaffold migration, inadequate apposition or compression of scaffold, inflation difficulties, rupture or pinhole of the delivery system balloon, deflation difficulties, withdrawal difficulties, embolization of catheter material.

Respiratory events:
Acute pulmonary edema, congestive heart failure, respiratory insufficiency or failure.

Vascular events:
Access site hematoma, hypotension/hypertension, pseudoaneurysm, arteriovenous fistula formation, retroperitoneal hematoma, vessel dissection or perforation, restenosis, thrombosis or occlusion, vasospasm, peripheral ischemia, dissection, distal embolization (air, tissue debris, thrombus).

Neurologic events:
Permanent (stroke) or reversible (TIA) neurologic event, femoral nerve injury, peripheral nerve injury.

Bleeding events:
Access site bleeding or hemorrhage, hemorrhage requiring transfusion or other treatment.

Allergic reactions to contrast media, antiplatelets, anticoagulants, the scaffold material, PLLA polymer matrix, sirolimus or sirolimus derivatives.

There is a possibility of adverse reactions of the body to the medicinal component of DREAMS. The exceedingly low quantity of sirolimus in blood plasma reduces the risk of the known side effects compared to systemic treatment. The following undesirable effects are known: Abnormal liver values, anaemia, joint pains, diarrhoea, hypercholesterolaemia, hypersensitivity reaction, including anaphylactic reaction, hypertriglyceridaemia, hypokalaemia, infections, interstitial pulmonary disease, lymphoma or other malignant diseases, thrombocytopenia.

The quantitative coronary angiography performed at 6 and 12 months follow-up poses some risks or inconveniences. They occur rarely, the most frequent events are bleedings, infection, and pain at the catheter insertion site, damage to blood vessels , allergic reaction to contrast media or medication. The use of X-ray radiation is necessary to carry out the angiogram. Experience with patients receiving similar treatment has shown that the total additional X-ray

radiation lasts between about 5-10 minutes. This corresponds to a radiation dose of about 4-6 millisievert (mSv; depending on X-ray system used); as a comparison: the average exposure to natural radiation per year amounts to about 2.5 mSv.

The additional diagnostic tests IVUS and OCT prolong the angiogram and you may be exposed to more X-ray radiation and contrast medium. These tests will be carried out during the coronary angiogram, so that no additional procedure is necessary.

The vasomotion test involves an infusion of acetylcholine, which can provoke a pathological narrowing of the vessel, which in turn may lead to chest pain, reduced blood supply to the heart, cardiac arrhythmia or an occlusion of the blood vessel. As the vasomotion test is performed during the coronary angiogram, these side effects are generally easily controlled.

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Subject is >= 18 years and <= 80 years of age
2. Written subject informed consent available prior to PCI
3. Subjects with stable or unstable angina pectoris or documented silent ischemia
4. Subject eligible for PCI
5. Subject acceptable candidate for coronary artery bypass surgery
6. Subjects with a maximum of two single lesions in two separate coronary arteries which have to be de novo lesions.
7. Reference vessel diameter between 2.2-3.8 mm by visual estimation, depending on the scaffold size used.
8. Target lesion length <= 21 mm by visual estimation, depending on the scaffold size used.
9. Target lesion stenosis by visual estimation, assisted by QCA / IVUS: >= 50% - < 100%
10. Eligible for Dual Anti Platelet Therapy (DAPT)

Exclusion criteria

1. Pregnant or breast-feeding females or females who intend to become pregnant during the time of the study
2. Evidence of myocardial infarction within 72 hours prior to index procedure
3. Subjects with a >=2 fold CK level or in absence of CK a >=3 fold CKMB level above the upper range limit within 24 hours prior to the procedure
4. Unprotected left main coronary artery disease
5. Three-vessel coronary artery disease at time of procedure
6. Thrombus in target vessel
7. Subject is currently participating in another study with an investigational device or an investigational drug and has not reached the primary endpoint yet
8. Planned interventional treatment of any non-target vessel within 30 days post-procedure
9. Subjects on dialysis
10. Planned intervention of the target vessel within 6-month after the index procedure
11. Ostial target lesion (within 5.0 mm of vessel origin)
12. Target lesion involves a side branch >2.0 mm in diameter
13. Documented left ventricular ejection fraction (LVEF) <= 30%
14. Heavily calcified lesion
15. Target lesion is located in or supplied by an arterial or venous bypass graft
16. The target lesion requires treatment with a device other than the pre-dilatation balloon or cutting/scoring balloon prior to scaffold placement (including but not limited to rotational atherectomy, etc.)
17.Unsuccessful pre-dilatation, defined as minimal lumen diameter smaller than the respective crossing profile of DREAMS and angiographic complications (e.g. distal embolization, side branch closure, extensive dissections that can*t be covered by a single scaffold), by visual estimation

18. Known allergies to: Acetylsalicylic Acid (ASA), Heparin, Contrast medium, Sirolimus, or similar drugs; or the scaffold material
19. Impaired renal function (serum creatinine > 2.5 mg/dl or 221 mmol/l, determined within 72 hours prior to intervention)
20. Subject is receiving oral or intravenous immuno-suppressive therapy (e.g., inhaled steroids are not excluded) or has known life-limiting immunosuppressive or autoimmune disease (e.g., human immunodeficiency virus, systemic lupus erythematosus, but not including diabetes mellitus)
21. Proximal or distal to the target lesion located stenosis that might require future revascularization or impede run off detected during diagnostic angiography
22. Life expectancy less than 1 year
23. Planned surgery or dental surgical procedure within 6 months after index procedure
24. In the investigators opinion subjects will not be able to comply with the follow-up requirements

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-02-2014
Enrollment:	20
Type:	Actual

Medical products/devices used

Generic name:	DREAMS;drug-eluting absorbable metal scaffold
Registration:	No

Ethics review

Approved WMO Date:	09-10-2013
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-05-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-06-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-10-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-05-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-09-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-11-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-06-2018
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT01960504
CCMO	NL45338.044.13